SEQENCE LISTING

<110> Kabushiki Kaisha Hayashibara Seibutsu Kagaku Kenkyujo

<120> Biologically-active conjugate

<130> US945

<160> 14

<210> 1
<211> 157
<212> PRT
<213> human

<400> 1

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 1               5                  10                  15
Val Ala Asn Pro Gln Ala Glu Gly Gln Leu Gln Trp Leu Asn Arg Arg
            20                  25                  30
Ala Asn Ala Leu Leu Ala Asn Gly Val Glu Leu Arg Asp Asn Gln Leu
        35                  40                  45
Val Val Pro Ser Glu Gly Leu Tyr Leu Ile Tyr Ser Gln Val Leu Phe
    50                  55                  60
Lys Gly Gln Gly Cys Pro Ser Thr His Val Leu Leu Thr His Thr Ile
65                  70                  75                  80
Ser Arg Ile Ala Val Ser Tyr Gln Thr Lys Val Asn Leu Leu Ser Ala
                85                  90                  95
Ile Lys Ser Pro Cys Gln Arg Glu Thr Pro Glu Gly Ala Glu Ala Lys
            100                 105                 110
Pro Trp Tyr Glu Pro Ile Tyr Leu Gly Gly Val Phe Gln Leu Glu Lys
        115                 120                 125
Gly Asp Arg Leu Ser Ala Glu Ile Asn Arg Pro Asp Tyr Leu Asp Phe
    130                 135                 140
Ala Glu Ser Gly Gln Val Tyr Phe Gly Ile Ile Ala Leu
145                 150                 155
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<210> 2
<211> 157
<212> PRT
<213> Artificial Sequence

<220>
<223> Variant protein of human tumor necrosis factor

<400> 2
Val Arg Ser Ser Ser Arg Thr Pro Ser Asp Xaa Pro Val Ala His Val
1 5 10 15
Val Ala Asn Pro Gln Ala Glu Gly Gln Leu Gln Trp Leu Asn Arg Arg
20 25 30
Ala Asn Ala Leu Leu Ala Asn Gly Val Glu Leu Arg Asp Asn Gln Leu
35 40 45
Val Val Pro Ser Glu Gly Leu Tyr Leu Ile Tyr Ser Gln Val Leu Phe
50 55 60
Xaa Gly Gln Gly Cys Pro Ser Thr His Val Leu Leu Thr His Thr Ile
65 70 75 80
Ser Arg Ile Ala Val Ser Tyr Gln Thr Xaa Val Asn Leu Leu Ser Ala
85 90 95
Ile Xaa Ser Pro Cys Gln Arg Glu Thr Pro Glu Gly Ala Glu Ala Xaa
100 105 110
Pro Trp Tyr Glu Pro Ile Tyr Leu Gly Gly Val Phe Gln Leu Glu Xaa
115 120 125
Gly Asp Arg Leu Ser Ala Glu Ile Asn Arg Pro Asp Tyr Leu Asp Phe
130 135 140
Ala Glu Ser Gly Gln Val Tyr Phe Gly Ile Ile Ala Leu
145 150 155

<210> 3
<211> 157
<212> PRT
<213> Artificial Sequence

<220>
<223> Variant protein of human tumor necrosis factor

<400> 3
Val Arg Ser Ser Ser Arg Thr Pro Ser Asp Met Pro Val Ala His Val
1 5 10 15
Val Ala Asn Pro Gln Ala Glu Gly Gln Leu Gln Trp Leu Asn Arg Arg
20 25 30
Ala Asn Ala Leu Leu Ala Asn Gly Val Glu Leu Arg Asp Asn Gln Leu
35 40 45
Val Val Pro Ser Glu Gly Leu Tyr Leu Ile Tyr Ser Gln Val Leu Phe
50 55 60
Ser Gly Gln Gly Cys Pro Ser Thr His Val Leu Leu Thr His Thr Ile
65 70 75 80
Ser Arg Ile Ala Val Ser Tyr Gln Thr Pro Val Asn Leu Leu Ser Ala
85 90 95
Ile Arg Ser Pro Cys Gln Arg Glu Thr Pro Glu Gly Ala Glu Ala Asn
100 105 110
Pro Trp Tyr Glu Pro Ile Tyr Leu Gly Gly Val Phe Gln Leu Glu Pro
115 120 125
Gly Asp Arg Leu Ser Ala Glu Ile Asn Arg Pro Asp Tyr Leu Asp Phe
130 135 140
Ala Glu Ser Gly Gln Val Tyr Phe Gly Ile Ile Ala Leu
145 150 155

<210> 4
<211> 92
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide used as primer with NNS sequence

<400> 4
tctactccca ggtcctcttc nnsggccaag gctgcccctc cacccatgtg ctcctcaccc 60

acaccatcag ccgcatcgcc gtctcctacc ag

<210> 5
<211> 90
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide used as primer with NNS sequence

<400> 5
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gacsnnggtc tggtaggaga cggcgatgcg

<210> 6
<211> 110
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide used as primer with NNS sequence

<400> 6
tagtcgggcc gattgatctc agcgctgagt cggtcaccsn nctccagctg gaagacccct 60
cccagataga tgggctcata ccagggsnng gcctcagccc cctctggggt

<210> 7
<211> 95
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide used as primer with NNS sequence

<400> 7
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ccccgagtga cnnscctgta gcccatgttg tagca

<210> 8
<211> 49
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide used as primer with NNS sequence

<400> 8
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<210> 9
<211> 36
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide used as primer with NNS sequence

<400> 9
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<210> 10
<211> 58
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide used as linker to insert into an expression vector a cDNA coding
a variant protein of human tumor necrosis factor

<400> 10
gtttaacttt aagaaggaga tatacatatg gtcagatcat cttctcgaac cccgagtg

<210> 11
<211> 59
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide used as linker to insert into an expression vector a cDNA coding
a variant pritein of human tumor necrosis factor

<400> 11
cttcctttcg ggctttgtta gcagccgaat tccagggcaa tgatcccaaa gtagacctg

<210> 12
<211> 471
<212> DNA
<213> Artificial Sequence

<220>
<223> DNA coding a variant protein of human tumor necrosis factor

<400> 12
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1 5 10 15
gta gca aac cct caa gct gag ggg cag ctc cag tgg ctg aac cgc cgg 96
Val Ala Asn Pro Gln Ala Glu Gly Gln Leu Gln Trp Leu Asn Arg Arg
20 25 30
gcc aat gcc ctc ctg gcc aat ggc gtg gag ctg aga gat aac cag ctg 144
Ala Asn Ala Leu Leu Ala Asn Gly Val Glu Leu Arg Asp Asn Gln Leu
35 40 45
gtg gtg cca tca gag ggc ctg tac ctc atc tac tcc cag gtc ctc ttc 192
Val Val Pro Ser Glu Gly Leu Tyr Leu Ile Tyr Ser Gln Val Leu Phe
50 55 60
tcg ggc caa ggc tgc ccc tcc acc cat gtg ctc ctc acc cac acc atc 240

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Ser Gly Gln Gly Cys Pro Ser Thr His Val Leu Leu Thr His Thr Ile
 65                  70                  75                  80
agc cgc atc gcc gtc tcc tac cag acc ccc gtc aac ctc ctc tct gcc 288
Ser Arg Ile Ala Val Ser Tyr Gln Thr Pro Val Asn Leu Leu Ser Ala
                85                  90                  95
atc cgc agc ccc tgc cag agg gag acc cca gag ggg gct gag gcc aac 336
Ile Arg Ser Pro Cys Gln Arg Glu Thr Pro Glu Gly Ala Glu Ala Asn
            100                 105                 110
ccc tgg tat gag ccc atc tat ctg gga ggg gtc ttc cag ctg gag ccg 384
Pro Trp Tyr Glu Pro Ile Tyr Leu Gly Gly Val Phe Gln Leu Glu Pro
        115                 120                 125
ggt gac cga ctc agc gct gag atc aat cgg ccc gac tat ctc gac ttt 432
Gly Asp Arg Leu Ser Ala Glu Ile Asn Arg Pro Asp Tyr Leu Asp Phe
    130                 135                 140
gcc gag tct ggg cag gtc tac ttt ggg atc att gcc ctg
Ala Glu Ser Gly Gln Val Tyr Phe Gly Ile Ile Ala Leu
145                 150                 155
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<210> 13
<211> 471
<212> DNA
<213> Artificial Sequence

<220>
<223> DNA coding a variant protein of human tumor necrosis factor

<400> 14

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gtc aga tca tct tct cga acc ccg agt gac gcg cct gta gcc cat gtt 48
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  1               5                  10                  15
gta gca aac cct caa gct gag ggg cag ctc cag tgg ctg aac cgc cgg 96
Val Ala Asn Pro Gln Ala Glu Gly Gln Leu Gln Trp Leu Asn Arg Arg
             20                  25                  30
gcc aat gcc ctc ctg gcc aat ggc gtg gag ctg aga gat aac cag ctg 144
Ala Asn Ala Leu Leu Ala Asn Gly Val Glu Leu Arg Asp Asn Gln Leu
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         35                  40                  45
gtg gtg cca tca gag ggc ctg tac ctc atc tac tcc cag gtc ctc ttc 192
Val Val Pro Ser Glu Gly Leu Tyr Leu Ile Tyr Ser Gln Val Leu Phe
     50                  55                  60
tcg ggc caa ggc tgc ccc tcc acc cat gtg ctc ctc acc cac acc atc 240
Ser Gly Gln Gly Cys Pro Ser Thr His Val Leu Leu Thr His Thr Ile
 65                  70                  75                  80
agc cgc atc gcc gtc tcc tac cag acc cgc gtc aac ctc ctc tct gcc 288
Ser Arg Ile Ala Val Ser Tyr Gln Thr Arg Val Asn Leu Leu Ser Ala
                 85                  90                  95
atc gcc agc ccc tgc cag agg gag acc cca gag ggg gct gag gcc ctc 336
Ile Ala Ser Pro Cys Gln Arg Glu Thr Pro Glu Gly Ala Glu Ala Leu
            100                 105                 110
ccc tgg tat gag ccc atc tat ctg gga ggg gtc ttc cag ctg gag acc 384
Pro Trp Tyr Glu Pro Ile Tyr Leu Gly Gly Val Phe Gln Leu Glu Thr
        115                 120                 125
ggt gac cga ctc agc gct gag atc aat cgg ccc gac tat ctc gac ttt 432
Gly Asp Arg Leu Ser Ala Glu Ile Asn Arg Pro Asp Tyr Leu Asp Phe
    130                 135                 140
gcc gag tct ggg cag gtc tac ttt ggg atc att gcc ctg
Ala Glu Ser Gly Gln Val Tyr Phe Gly Ile Ile Ala Leu
145                 150                 155
```

<210> 14
<211> 157
<212> PRT
<213> Artificial Sequence

<220>
<223> Variant protein of human tumor necrosis factor

<400> 3

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Val Arg Ser Ser Ser Arg Thr Pro Ser Asp Ala Pro Val Ala His Val
 1               5                  10                  15
Val Ala Asn Pro Gln Ala Glu Gly Gln Leu Gln Trp Leu Asn Arg Arg
            20                  25                  30
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Ala Asn Ala Leu Leu Ala Asn Gly Val Glu Leu Arg Asp Asn Gln Leu
35 40 45
Val Val Pro Ser Glu Gly Leu Tyr Leu Ile Tyr Ser Gln Val Leu Phe
50 55 60
Ser Gly Gln Gly Cys Pro Ser Thr His Val Leu Leu Thr His Thr Ile
65 70 75 80
Ser Arg Ile Ala Val Ser Tyr Gln Thr Arg Val Asn Leu Leu Ser Ala
85 90 95
Ile Ala Ser Pro Cys Gln Arg Glu Thr Pro Glu Gly Ala Glu Ala Leu
100 105 110
Pro Trp Tyr Glu Pro Ile Tyr Leu Gly Gly Val Phe Gln Leu Glu Thr
115 120 125
Gly Asp Arg Leu Ser Ala Glu Ile Asn Arg Pro Asp Tyr Leu Asp Phe
130 135 140
Ala Glu Ser Gly Gln Val Tyr Phe Gly Ile Ile Ala Leu
145 150 155